

**RIBOSWITCHES, METHODS FOR THEIR USE,
AND COMPOSITIONS FOR USE WITH RIBOSWITCHES**

ABSTRACT OF THE DISCLOSURE

It has been discovered that certain natural mRNAs serve as metabolite-sensitive genetic switches wherein the RNA directly binds a small organic molecule. This binding process changes the conformation of the mRNA, which causes a change in gene expression by a variety of different mechanisms. Modified versions of these natural "riboswitches" (created by using various nucleic acid engineering strategies) can be employed as designer genetic switches that are controlled by specific effector compounds. Such effector compounds that activate a riboswitch are referred to herein as trigger molecules. The natural switches are targets for antibiotics and other small molecule therapies. In addition, the architecture of riboswitches allows actual pieces of the natural switches to be used to construct new non-immunogenic genetic control elements, for example the aptamer (molecular recognition) domain can be swapped with other non-natural aptamers (or otherwise modified) such that the new recognition domain causes genetic modulation with user-defined effector compounds. The changed switches become part of a therapy regimen—turning on, or off, or regulating protein synthesis. Newly constructed genetic regulation networks can be applied in such areas as living biosensors, metabolic engineering of organisms, and in advanced forms of gene therapy treatments.